

Cardiac Causes of Pulmonary Hypertension

Left ventricular failure from any cause increases pulmonary venous pressure and to some extent pulmonary arterial pressure. By contrast, mitral stenosis produces severe venous hypertension and significant pulmonary artery hypertension.

CARCINOMA OF THE LUNG

Carcinoma of the lung is the most common cause of death from cancer in the United States. The large majority (90%) of cancers of the lung are a consequence of cigarette smoking (see Chap. 8).

Squamous Cell Carcinoma

Squamous cell carcinoma has been for many years the most common variety of lung cancer in the United States and many other countries.

□ **Pathology:** Most squamous cell carcinomas arise in the central portion of the lung from the major or segmental bronchi. On gross examination, they tend to be firm, gray-white, ulcerated lesions that extend through the bronchial wall into the adjacent parenchyma (Fig. 12-35). The microscopic appearance of squamous cell carcinoma is highly variable. The range of differentiation extends from mature squamous cells with keratin pearls to an anaplastic lesion that is recognized as of squamous cell origin only by

electron microscopy and immunohistochemical examination. In well-differentiated tumors, keratin often occurs as "pearls," which appear as central, bright eosinophilic aggregates of keratin surrounded by "onion skin" layers of squamous cells.

Carcinomas of the lung of all histologic types metastasize most frequently to the regional lymph nodes, particularly the hilar and mediastinal nodes. The most common site of extranodal metastasis is the adrenal gland, although adrenal insufficiency is distinctly uncommon. Lung cancer not infrequently presents initially as metastatic disease, with the brain, bone, and liver being common sites.

□ **Clinical Features:** Most squamous cell carcinomas present with symptoms related to their bronchial origin: persistent cough, hemoptysis, or bronchial obstruction, the last accompanied by pulmonary infections (recurrent pneumonias, lung abscesses) or atelectasis. Extension of the tumor can cause compression of the superior vena cava, resulting in severe venous and lymphatic congestion of the upper part of the body (superior vena cava syndrome). Growth of a lung cancer (usually squamous) in the apex of the lung (Pancoast tumor) may extend to involve the eighth cervical and first and second thoracic nerves, which results in shoulder pain radiating in an ulnar distribution down the arm (Pancoast syndrome). A Pancoast tumor may also paralyze the cervical sympathetic nerves and cause Horner syndrome, characterized by depression of the eyeball (enophthalmos), ptosis of the upper eyelid, constriction of the pupil (miosis), and absence of sweating (anhidrosis) on the affected side. Pleural effusion is

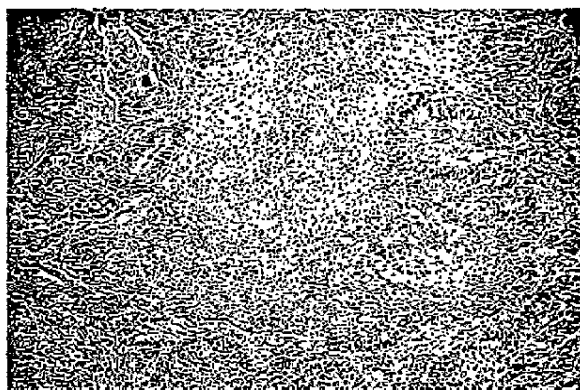


FIGURE 12-35

Squamous cell carcinoma of the lung. (A) A tumor mass arising from a proximal branch of the left mainstem bronchus (arrow) has occluded the bronchial lumen and metastasized to the regional lymph nodes. T, trachea. (B) Photomicrograph of a well-differentiated squamous cell carcinoma.

common and leads to dyspnea. Lymphangitic spread of the tumor within the lung may impair oxygenation. Invasion of the pericardium by cancer results in pericardial effusion and sometimes cardiac tamponade.

The median survival for untreated squamous cell carcinoma of the lung is less than a year. At the time of diagnosis, about 60% of all squamous carcinomas are deemed resectable, and the overall 5-year survival rate after surgery is 37%.

Adenocarcinoma

Adenocarcinoma of the lung has been increasing in frequency, particularly in women, and in many locations may be more common than squamous cell carcinoma. Adenocarcinoma of the lung tends to arise in the periphery, usually in the upper lobes, with puckering of the overlying pleura (Fig. 12-36). Most of these tumors occur in smokers, and fewer than 10% are associated with subpleural scars, secondary to old tuberculosis, healed infarcts, residual pneumonitis, or trauma.

Pathology: At initial presentation, adenocarcinomas of the lung appear as irregular masses 2 to 5 cm in diameter, although many are larger. On cut section, the tumor is grayish-white and often glistening, owing to the production of mucus. Histologically,

adenocarcinomas of the lung present a wide variety of morphologic patterns. The neoplastic cells may resemble dilated or nonciliated columnar epithelial cells, goblet cells, cells of the bronchial glands, or Clara cells. In the most common pattern, well-differentiated acinar carcinomas form regular glands, which are lined by columnar cells with basal nuclei (see Fig. 12-36). Papillary adenocarcinomas exhibit columnar to cuboidal cells and form a single layer on a core of fibrous connective tissue. Solid adenocarcinomas are poorly differentiated tumors, although in some there is a suggestion of gland formation. Mucus production in all varieties of adenocarcinoma varies from scant to abundant.

Adenocarcinomas metastasize readily to the same sites as do squamous cell carcinomas, but they tend to grow more rapidly and frequently invade the pleura. Less than 40% of adenocarcinomas can be resected, and the 5-year survival for these patients is only 25%.

Bronchioloalveolar Carcinoma

Bronchioloalveolar cancer is always peripheral in origin and, as the name indicates, derives from bronchiolar or alveolar epithelial cells. The tumor shows no relationship to tobacco smoking. Most of these cancers originate from Clara cells, although a minority are composed principally of type II pneumocytes.

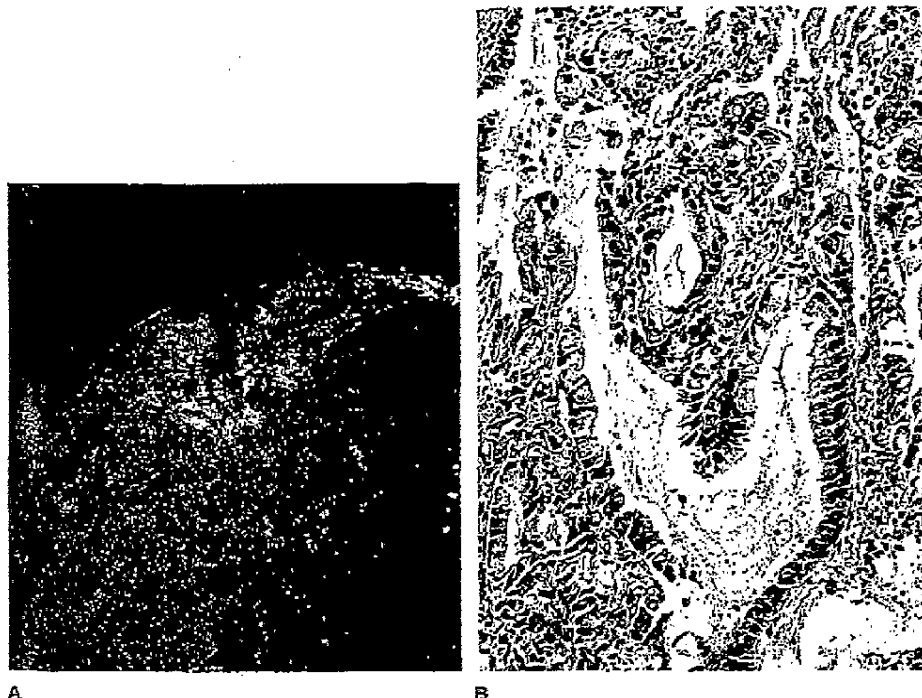


FIGURE 12-36
Adenocarcinoma of the lung.
(A) A peripheral tumor in the right upper lobe puckers the pleural surface. (B) A microscopic view shows a well-differentiated, mucus-producing adenocarcinoma.

On gross examination, bronchioloalveolar carcinoma presents as a single peripheral nodule, multiple nodules, or a diffuse infiltrate that resembles pneumonia. The cut section of the tumor is often mucoid and may not be recognized macroscopically as a tumor (Fig. 12-37). On microscopic examination, well-differentiated, mucin-containing columnar cells line the alveolar spaces without invading the stroma. However, tumors composed of neoplastic type II pneumocytes do not contain mucin.

When limited to a single lesion, the prognosis for bronchioloalveolar carcinoma is good. In the absence of lymph node metastases, the cure rate is more than 50%.

Small Cell Carcinoma

■ *Small cell carcinoma is a highly malignant lung cancer characterized by sheets of small tumor cells, which differentiate in the direction of neuroendocrine cells. This variant accounts for 10% to 20% of all lung cancers. More than 80% of the patients are men, and 90% are cigarette smokers. Small cell carcinoma is believed to arise from the pluripotential basal cells of the bronchial epithelium.*

In the majority of cases, small cell carcinoma originates near the hilum of the lung. On cut section, the tumor is soft, glistening, and grayish-white, often with areas of necrosis. Microscopically, in half of the cases the tumor cells are small and round or oval (Fig. 12-38), with dense hyperchromatic nuclei and scanty cytoplasm. The appearance is similar to that of lymphocytes (oat cells). A fourth of the tumors display

fusiform or elongated cells, and another fourth exhibit medium-sized, polygonal cells with abundant cytoplasm (intermediate cell variants).

The majority of patients with small cell carcinoma are symptomatic at the time of diagnosis, and two thirds of the tumors have already metastasized to bone, liver, brain, and other organs. Chemotherapy is the common treatment for disseminated small cell carcinoma, and recent advances have led to a dramatic improvement in prognosis. Tumors limited to the lung are treated by radiation.

Carcinoid Tumors

■ *Carcinoid tumors are a group of neuroendocrine pulmonary neoplasms derived from the pluripotential basal layer of the respiratory epithelium. They comprise less than 5% of primary lung tumors, show no sex predilection, and are not related to cigarette smoking. Although neuropeptides are readily demonstrated in the tumor cells, the large majority are endocrinologically silent. The tumor is of low-grade malignancy, but 5% to 10% metastasize to regional lymph nodes.*

Metastatic Tumors

The most common malignant neoplasm of the lung is a metastatic tumor. Metastatic tumors in the lung are typically multiple and circumscribed (Fig. 12-39) and are viewed radiologically as "cannon ball" metastases. The common primary sites are the breast, stomach, pancreas, and colon.

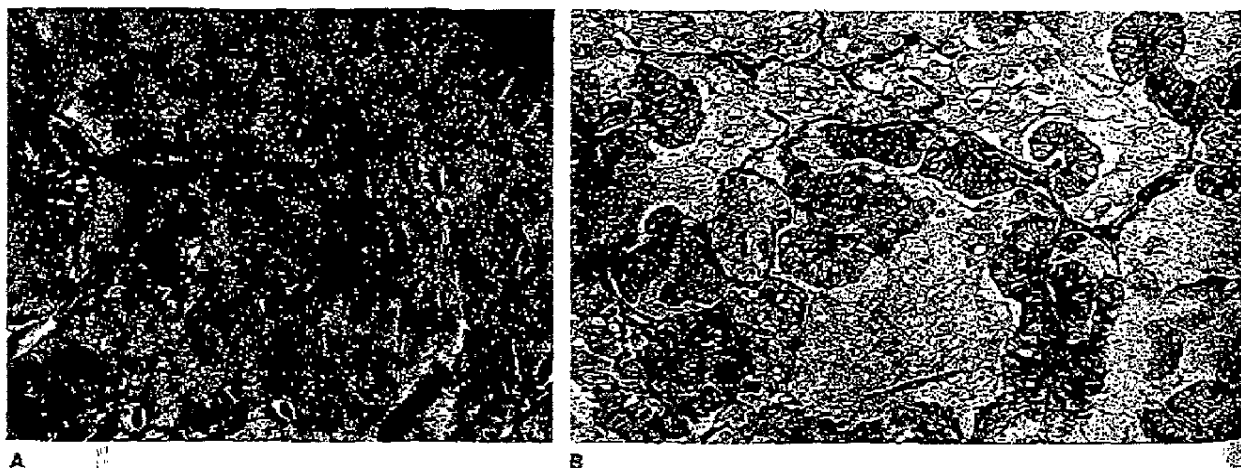


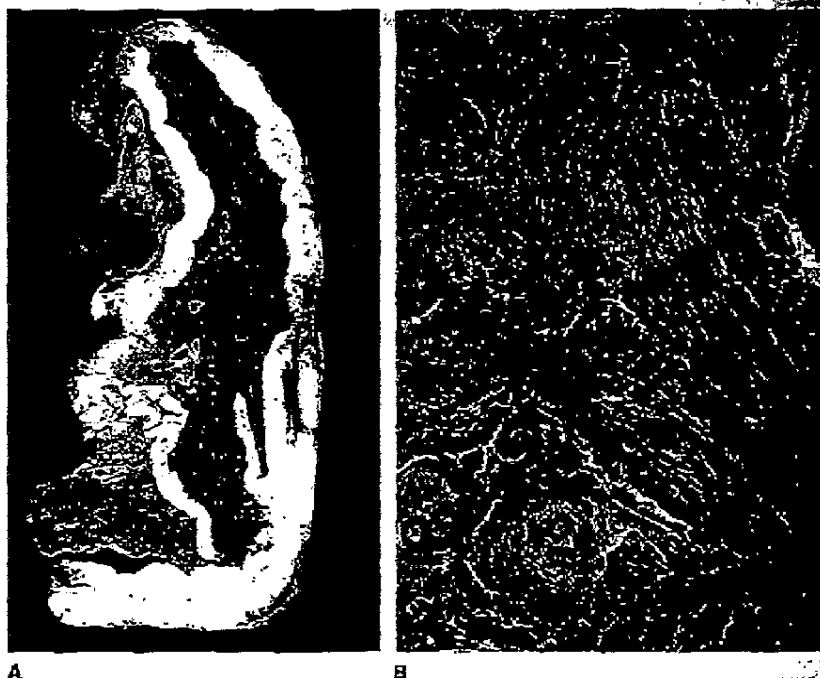
FIGURE 12-37

Bronchioloalveolar carcinoma. (A) The cut surface of the lung is solid, glistening, and mucoid, an appearance that reflects a diffusely infiltrating tumor. (B) A microscopic view shows alveoli lined by columnar, mucus-producing tumor cells and filled with mucus.

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FIGURE 12-40

Pleural mesothelioma. (A) The lung is encased by a dense pleural tumor that extends into the fissures. (B) A microscopic view shows the sarcomatous and epithelial components of the tumor.



results from infections of the pleura. It is commonly a complication of bacterial pneumonia that extends to the pleural surface, the classic example of which is pneumococcal pneumonia.

Empyema is a variant of pyothorax in which thick pus accumulates within the pleural cavity, often with loculation and fibrosis.

Hemothorax refers to the accumulation of blood in the pleural cavity as a result of trauma or rupture of a vessel, for example dissecting aneurysm of the aorta.

Chylothorax is the accumulation in the pleural cavity of a milky, lipid-rich fluid (chyle) as a result of lymphatic obstruction. It has an ominous portent, because obstruction of the lymphatics suggests disease of the lymph nodes in the posterior mediastinum.

MESOTHELIOMA

■ *Mesothelioma* is a malignant tumor of mesothelial cells that is most common in the pleura but also occurs in the peritoneum and the tunica vaginalis of the testis. Most

pleural and peritoneal mesotheliomas are related to asbestos exposure (see discussion earlier on asbestos-related diseases), although some patients deny contact with this mineral. The tumors are typically encountered in middle-aged men occupationally exposed to asbestos, even for a short time.

□ **Pathology:** On gross examination pleural mesothelioma characteristically encases and compresses the lung, extending into fissures and interlobar septa (Fig. 12-40). Microscopically, classic mesothelioma exhibits a biphasic appearance, namely epithelial and sarcomatous patterns. Glands and tubules that resemble adenocarcinoma are admixed with sheets of spindle cells that are similar to a fibrosarcoma.

□ **Clinical Features:** Patients with pleural mesothelioma present with a pleural effusion or with pleural mass, chest pain, and dyspnea. The lesion may be limited to the thorax, but in about a fourth of the cases metastases appear elsewhere. Treatment is ineffective and the prognosis is hopeless.